



NOTES

INFLAMMATORY BOWEL DISEASE

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Immune-mediated inflammatory bowel conditions
- More common in White people of Jewish descent
- Usually presents in young people, 15–35
- Up to 25% of people with inflammatory bowel disease have affected first-degree relative

CAUSES

- Gut microbiome alterations
- “Western” style diet: high processing/sugar/fat content

RISK FACTORS

- Crohn’s disease: smoking
 - Smoking may be protective for Ulcerative colitis

SIGNS & SYMPTOMS

- Chronic diarrhea, frequently bloody/mucous
- Abdominal pain
- Fever, weight loss, anemia
- Extraintestinal manifestations
 - Arthritis, uveitis

DIAGNOSIS

DIAGNOSTIC IMAGING

- Endoscopy

LAB RESULTS

- Biopsy

TREATMENT

MEDICATIONS

- Anti-inflammatory medications; antibiotics; immunosuppressants

SURGERY

- Surgical resection

OTHER INTERVENTIONS

- Dietary changes

VISIT...

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CROHN'S DISEASE

osms.it/crohns-disease

PATHOLOGY & CAUSES

- AKA Crohn disease, regional enteritis
- Chronic, immune-related disorder → excessive immune response to unknown trigger → transmural inflammation anywhere along gastrointestinal (GI) tract, mouth to anus
- Compare to ulcerative colitis
 - Only affects colon, rectum; superficial lesions; **autoimmune disorder** where tissue is directly attacked by immune system
- Frameshift mutation in nucleotide-binding oligomerization domain-containing protein 2 (NOD2)/ caspase recruitment domain-containing protein 15 (CARD15)
 - Excessive inflammatory response → tissue damage
- Unknown immune response trigger → T helper (Th) 1 cells release inflammatory cytokines
 - Interferon (IFN) gamma, tumor necrosis factor (TNF) alpha → inflammatory response → cytokines recruit macrophages → further inflammatory mediators released (proteases, platelet activating factor, free radicals) → further inflammation → healthy tissue destroyed → **inflammatory cells invade intestinal mucosa** → ulcer, granuloma form → transmural inflammation → intestinal lumen; fistula formation, narrowing
- **Fistula, stricture formation**
 - Serosal layer involvement → fistula
 - **Most common:** enterovesical, enterocutaneous, enterovaginal, enteroenteric fistulae
- Scattered inflammation → **cobblestone** appearance
- Most commonly affects **terminal ileum, colon**

CAUSES

- Unclear; mycobacterium paratuberculosis, pseudomonas, listeria implicated

SIGNS & SYMPTOMS

- Unpredictable patterns of flares, remissions
- Abdominal pain; most common in right lower quadrant (ileal inflammation)
- Fatigue, fever, nausea, vomiting
- **Chronic diarrhea**; may/may not be bloody
 - Gross bleeding rare; upon microscopy, bleeding common
- **Malabsorption, weight loss, vitamin deficiencies**
- Up to 20% of cases present with **inflammatory eye, skin, joint lesions**
 - **Uveitis, erythema nodosum, pyoderma gangrenosum**, cholelithiasis (impaired bile reabsorption), arthritis
- **Perianal abscesses**, phlegmon, fistulae
 - **Perianal fistulas** (up to 30%)
 - **Enterovesical fistulae** → recurrent UTI, pneumaturia
 - **Enteroenteric fistulae** → asymptomatic
 - **Enterovaginal fistulae** → passage of fecal matter through vagina
 - **Enterocutaneous fistulae** → draining of bowel contents unto skin
- Intestinal obstruction (up to 30%)



Figure 33.1 Pyoderma gangrenosum on the leg of an individual with Crohn's disease.

**MNEMONIC: CHRISTMAS****Features of Crohn's disease**

- C**obblestones
- H**igh temperature
- R**educed lumen
- I**ntestinal fistulae
- S**kip lesions
- T**ransmural: all layers, may ulcerate
- M**alabsorption
- A**bdominal pain
- S**ubmucosal fibrosis

DIAGNOSIS**DIAGNOSTIC IMAGING**

- Endoscopy

LAB RESULTS

- Biopsy
 - Cobblestone appearance, intermittent lesion pattern, pseudopolyps, aphthous ulcers

OTHER DIAGNOSTICS

- Barium enema

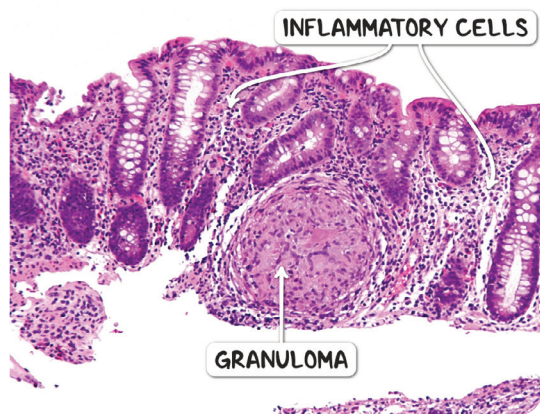


Figure 33.2 Histological appearance of Crohn's disease. The lamina propria is expanded by chronic inflammatory cells and there is a non-caseating granuloma present.

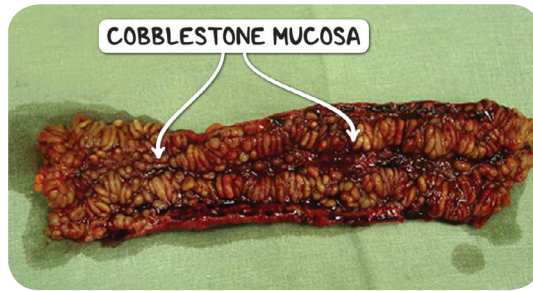


Figure 33.3 Gross pathology of a resected colon involved by Crohn's disease. The severe and prolonged inflammation has led to a cobblestone appearance of the colonic mucosa.

TREATMENT**MEDICATIONS**

- Anti-inflammatory medications → sulfasalazine
 - For colonic symptom management
- **Antibiotics** → metronidazole
 - Reduce bacterial overgrowth, anti-inflammatory effect
- **Immunosuppressants** → prednisone, azathioprine
 - Only if no response to antibiotics
- Antidiarrheals
- Methotrexate, anti-TNF agents
 - Refractory disease

SURGERY

- Surgical removal of affected tissue
 - High relapse rate
 - **Short bowel syndrome**: complication of resection

OTHER INTERVENTIONS

- Nutritional supplementation, support

MICROSCOPIC COLITIS

osms.it/microscopic-colitis

PATHOLOGY & CAUSES

- Idiopathic **chronic inflammation of colon** → watery diarrhea
- Associated with **celiac disease**, autoimmune diseases, NSAIDs, smoking
- More common in individuals who are biologically female
- Unknown trigger → **abnormal collagen metabolism** → dysfunctional epithelium → alteration in barrier function → mucosal inflammation → decreased sodium absorption, increased chloride secretion → secretory diarrhea

TYPES

Collagenous

- More common in older individuals who are biologically female
- Dense subepithelial collagenous layer; increased intraepithelial lymphocytes, inflammatory infiltrate in lamina propria

Lymphocytic

- Increased intraepithelial lymphocytes, inflammatory infiltrate in lamina propria

SIGNS & SYMPTOMS

- Abdominal pain
- Chronic watery diarrhea
- No weight loss
- Fecal urgency, incontinence
- Anemia

DIAGNOSIS

DIAGNOSTIC IMAGING

Endoscopy

- Non-specific findings, normal mucosa

LAB RESULTS

- Biopsy of colonic mucosa
 - Inflammatory changes in lamina propria, intraepithelial lymphocytic infiltration, dense subepithelial collagenous layer
- Elevated inflammatory markers (nonspecific)
 - Erythrocyte sedimentation rate, myeloperoxidase
- Autoantibodies
 - Anti-thyroid peroxidase (TPO), antinuclear (ANA), antineutrophil cytoplasmic (ANCA), anti *Saccharomyces cerevisiae* (ASCA), rheumatoid factor (RF)

TREATMENT

MEDICATIONS

- Avoid NSAIDs, other medications associated with microscopic colitis
- Antidiarrheals
 - Loperamide, bismuth salicylate
- Corticosteroids
 - Budesonide, prednisone
- Bile acid sequestrants
 - Cholestyramine

SURGERY

- Surgical resection (ileostomy)

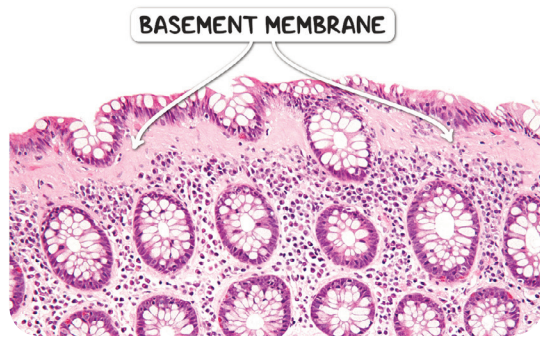


Figure 33.4 Histological appearance of collagenous colitis. The subepithelial basement membrane is markedly thickened.

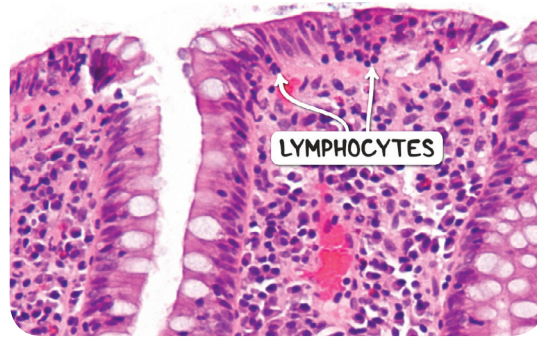


Figure 33.5 Histological appearance of lymphocytic colitis. There is an increase in the number of intraepithelial lymphocytes ($>20/100$ epithelial cells).

PROTEIN LOSING ENTEROPATHY

osms.it/protein-losing-enteropathy

PATHOLOGY & CAUSES

- Inflammatory GI conditions → **loss of serum proteins into GI tract**
- Mucosal injury → epithelial inflammation, → **mucosal permeability** → protein exudates across epithelium → proteins in GI tract degraded into amino acids (AA)
- Lymphatic obstruction/venous stasis → increased hydrostatic pressure in lymphatics → **lymph leaks into intestinal lumen** → reduced chylomicron reabsorption → decrease in fat soluble vitamins → protein deficiency

CAUSES

- Inflammatory bowel disease
 - **Crohn's disease, ulcerative colitis**
- Malabsorptive diseases
 - Tropical sprue, celiac sprue
- Infectious diseases
 - *C. difficile* → pseudomembranous colitis
- GI malignancies

SIGNS & SYMPTOMS

- Hyponatremia, peripheral edema, ascites
- Serosal effusions (pleural and pericardial)
 - Dyspnea, cough, chest pain
- Steatorrhea, bloating, flatulence, abdominal pain
- Weight loss, chronic diarrhea

DIAGNOSIS

LAB RESULTS

- Consider in individuals with edema, hypoalbuminemia
- Increase in alpha-1 antitrypsin clearance
- Exclude other causes of hypoproteinemia
 - Renal disease → proteinuria
 - Hepatic disease → impaired protein synthesis
 - Malnutrition

TREATMENT

OTHER INTERVENTIONS

- Low fat, high protein diet; supplement medium chain triglycerides (MCT)

ULCERATIVE COLITIS

osms.it/ulcerative-colitis

PATHOLOGY & CAUSES

- Autoimmune disease → **superficial ulcer formation**; continuous, circumferential inflammation in colonic, rectal mucosa
- Most common inflammatory bowel disease; may present at any age
- Compare to Crohn's disease
 - Usually affects young people, affects entire GI tract; causes transmural inflammation; patches of inflamed mucosa, cobblestone appearance
- **CD8+ cell activation** → destruction of cells in mucosal, submucosal colonic layers
 - Associated with perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCAs)
- Multifactorial origin
 - Environmental stimuli + excessive sulfide-producing bacteria + genetic predisposition
- More common among white people, especially of Eastern European descent
- More common in young individuals who are biologically female

CAUSES

- Unclear; autoimmune reaction against colonic flora, molecular mimicry, increased sulfide production implicated
- Environmental factors contribute to acute flares

COMPLICATIONS

- **Toxic megacolon, anal fissures, perirectal abscess**



MNEMONIC: ULCERATIONS

Features of Ulcerative colitis

Ulcers

Large intestine

Carcinoma (risk of)

Extraintestinal manifestations

Remnants of old ulcers
(pseudopolyps)

Abscesses in crypts

Toxic megacolon (risk of)

Inflamed, red, granular mucosa

Originates at rectum

Neutrophil invasion

Stool is bloody

SIGNS & SYMPTOMS

- Acute flares, remissions; gradual onset
 - Risk of relapse related to person's age at diagnosis
- Severity determined by frequency of bowel movements, degree of inflammation, systemic symptoms
- Colicky, left lower quadrant pain
- **Diarrhea**; frequently grossly bloody, mucous
- **Rectal tenesmus**, incontinence, urgency, bleeding
 - **Tenesmus**: Latin teinesmos; to strain
- Fever, fatigue, weight loss, anemia, dehydration
- Extraintestinal manifestations
 - **Arthritis** (most common); uveitis; erythema nodosum; pyoderma gangrenosum; primary sclerosing cholangitis; arterial, venous thromboembolisms

DIAGNOSIS

- > four weeks active diarrhea + inflammatory findings on endoscopy + chronic inflammatory changes on biopsy
- Biopsy
 - Crypt abscesses

LAB RESULTS

- Anemia
- Elevated inflammatory markers
 - Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)

OTHER DIAGNOSTICS

- Clinical diagnosis; exclude other causes of colitis
 - Infections (e.g. parasites, *Clostridium difficile*), STIs, radiation, medications

TREATMENT

MEDICATIONS

- Anti-inflammatory medications
 - Sulfasalazine, mesalamine
- Immunosuppressors
 - Corticosteroids, azathioprine, cyclosporine
- TNF blocking agent

SURGERY

- Colectomy only if disease localized



Figure 33.8 The clinical appearance of erythema nodosum; a cutaneous manifestation of inflammatory bowel disease.

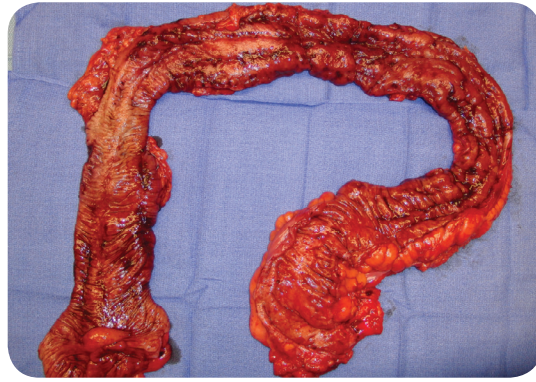


Figure 33.6 A pancolectomy specimen from an individual with ulcerative colitis.

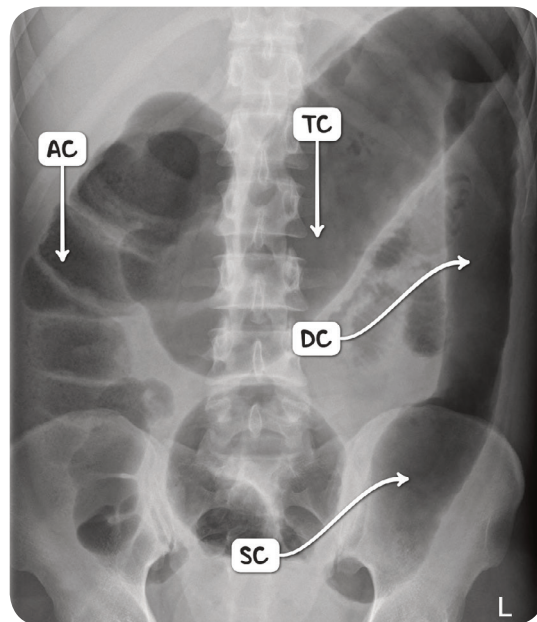


Figure 33.7 Abdominal radiograph demonstrating toxic megacolon, a complication of ulcerative colitis.

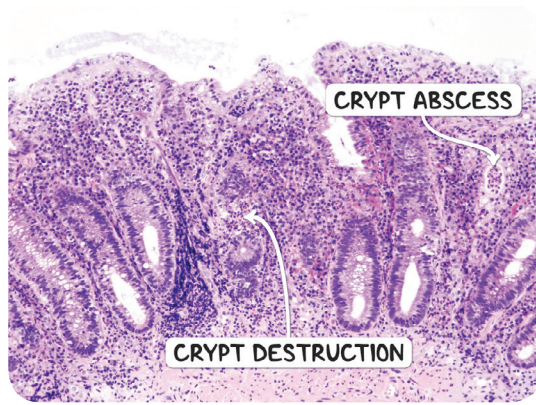


Figure 33.9 Histological appearance of active ulcerative colitis in a colonic biopsy. There is active inflammation causing crypt destruction. Cryptitis and crypt abscesses are also present.

CROHN'S DISEASE VS ULCERATIVE COLITIS

	CROHN'S DISEASE	ULCERATIVE COLITIS
PRESENTATION AGE	15-35	Throughout lifespan
SITE OF APPEARANCE	Mouth to anus	Colonic, rectal mucosa
TYPE OF LESION	Transmural inflammation	Superficial ulcers
MICROSCOPIC FINDINGS	Non-caseating granulomas	Crypt ulcers, abscesses
CHARACTERISTIC PATTERN	Skip lesions	Continuous lesions
CHARACTERISTIC APPEARANCE	Cobblestone pattern, creeping fat, string sign on barium x-rays	Loss of haustra on imaging (lead pipe appearance), friable mucosa
CLINICAL PRESENTATION	Right lower quadrant pain fistulas, phlegmon	Left lower quadrant pain Gross bleeding
DISEASE MECHANISM	Transmural inflammation along GI tract	Destruction of colonic mucosa, submucosa
TREATMENT	Corticosteroids, azathioprine, metronidazol, infliximab, adalimumab	Mesalamine, infliximab, surgical resection